SEQUENCE LISTING

<110> CO, MAN SUNG
VASQUEZ, MAXIMILIANO
CARRENO, BEATRIZ
CELNIKER, ABBIE CHERYL
COLLINS, MARY
GOLDMAN, SAMUEL
GRAY, GARY S.
KNIGHT, ANDREA
O'HARA, DENISE
RUP, BONITA
VELDMAN, GEERTRUIDA M.

<120> HUMANIZED IMMUNOGLOBULIN REACTIVE WITH B7-2 AND METHODS OF TREATMENT THEREWITH

<130> 08702.0081-00000

<140> 09/249,011
<141> 1999-02-12

<160> 24

<170> PatentIn Ver. 2.1

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<220>
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<222> (1)..(405)
<223> Anti-B7-2 heavy chain

<400> 1

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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
  1               5                  10                  15

gtg cac tcc cag gtc cag ctg cag cag tct ggg cct gag ctg gtg agg   96
Val His Ser Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg
            20                  25                  30

cct ggg gaa tca gtg aag att tcc tgc aag ggt tcc ggc tac aca ttc   144
Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe
        35                  40                  45

act gat tat gct ata cag tgg gtg aag cag agt cat gca aag agt cta   192
Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu
    50                  55                  60

gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac   240
Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
65                  70                  75                  80
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cag aag ttt aag ggc aag gcc aca atg act gta gac aaa tcc tcc agc   288
Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser
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aca gcc tat atg gaa ctt gcc aga ttg aca tct gag gat tct gcc atc   336
Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile
            100                 105                 110

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa gga   384
Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

acc tca gtc acc gtc tcc tca                                      405
Thr Ser Val Thr Val Ser Ser
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<213> Murine sp.

<220>
<223> Anti-B7-2 heavy chain

<400> 2

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  1               5                  10                  15

Val His Ser Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg
             20                  25                  30

Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe
         35                  40                  45

Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu
     50                  55                  60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
 65                  70                  75                  80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser
                85                  90                  95

Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile
            100                 105                 110

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Ser Val Thr Val Ser Ser
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<210> 3
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<213> Murine sp.

<220>
<221> CDS
<222> (1)..(396)
<223> Anti-B7-2 light chain

<400> 3

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Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser
  1               5                  10                  15

ggt acc tgt ggg gac att gtg ctg tca cag tct cca tcc tcc ctg gct   96
Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala
             20                  25                  30

gtg tca gca gga gag aag gtc act atg agc tgc aaa tcc agt cag agt   144
Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser
         35                  40                  45

ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag   192
Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
     50                  55                  60

aaa cca ggg cag tct cct aaa ctg ctg atc tac tgg gca tcc act agg   240
Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
 65                  70                  75                  80

gaa tct ggg gtc cct gat cgc ttc aca ggc agt gga tct ggg aca gat   288
Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
                 85                  90                  95

ttc act ctc acc atc agc agt gtg cag gct gaa gac ctg gca gtt tat   336
Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr
            100                 105                 110

tac tgc acg caa tct tat aat ctt tac acg ttc gga ggg ggg acc aag   384
Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys
        115                 120                 125

ctg gaa ata aaa                                                  396
Leu Glu Ile Lys
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<210> 4
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<212> PRT
<213> Murine sp.

<220>
<223> Anti-B7-2 light chain

<400> 4

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Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala
             20                  25                  30
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Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser
        35                  40                  45

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
    50                  55                  60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
65                  70                  75                  80

Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
                85                  90                  95

Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr
            100                 105                 110

Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys
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<210> 5
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<212> DNA
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B4

<220>
<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 heavy chain

<220>
<221> CDS
<222> (1)..(405)

<400> 5

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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
  1               5                  10                  15

gtg cac tcc cag gtc cag ctg gtg cag tct ggg gct gag gtg aag aag   96
Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30

cct ggg agc tca gtg aag gtg tcc tgc aaa gct tcc ggc tac aca ttc  144
Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45

act gat tat gct ata cag tgg gtg aga cag gct cct gga cag ggc ctc  192
Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
    50                  55                  60

gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac  240
Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
65                  70                  75                  80
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```
cag aag ttt aag ggc aag gcc aca atg act gta gac aag tcg acg agc   288
Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
                85                  90                  95

aca gcc tat atg gaa ctt agt tct ttg aga tct gag gat acg gcc gtt   336
Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
            100                 105                 110

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa ggt   384
Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

acc ctt gtc acc gtc tcc tca                                      405
Thr Leu Val Thr Val Ser Ser
    130                 135
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<210> 6
<211> 135
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 heavy chain

B4

<400> 6

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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
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Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45

Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
    50                  55                  60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
65                  70                  75                  80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
                85                  90                  95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Leu Val Thr Val Ser Ser
    130                 135
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<210> 7
<211> 396

<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 light chain

<220>
<221> CDS
<222> (1)..(396)

<400> 7

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atg gat tca cag gcc cag gtt ctt ata ttg ctg ctg cta tgg gta tct   48
Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser
  1               5                  10                  15

ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat tcc ctg gct   96
Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala
             20                  25                  30

gta agc tta gga gag agg gcc act att agc tgc aaa tcc agt cag agt  144
Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
         35                  40                  45

ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag  192
Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
     50                  55                  60

aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca tcc act agg  240
Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
 65                  70                  75                  80

gaa tct ggg gtc cct gat cgc ttc agt ggc agt gga tct ggg aca gat  288
Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                 85                  90                  95

ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg gca gtt tat  336
Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
            100                 105                 110

tac tgc acg caa tct tat aat ctt tac acg ttc gga cag ggg acc aag  384
Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

gtg gaa ata aaa                                                 396
Val Glu Ile Lys
    130
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<210> 8
<211> 132
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 light chain

<400> 8
Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser
1 5 10 15

Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala
20 25 30

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
35 40 45

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
50 55 60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
100 105 110

Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
115 120 125

Val Glu Ile Lys
130

B4

<210> 9
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR1 of humanized murine anti-human B7-2 heavy chain

<220>
<221> CDS
<222> (1)..(15)

<400> 9
gat tat gct ata cag 15
Asp Tyr Ala Ile Gln
1 5

<210> 10
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR1 of humanized murine anti-human B7-2 heavy chain

<400> 10
Asp Tyr Ala Ile Gln
1 5

<210> 11
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR2 of humanized murine anti-human B7-2 heavy chain

<220>
<221> CDS
<222> (1)..(51)

<400> 11
gtt att aat att tac tat gat aat aca aac tac aac cag aag ttt aag 48
Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
1 5 10 15

ggc 51
Gly

B4

<210> 12
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR2 of humanized murine anti-human B7-2 heavy chain

<400> 12
Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 13
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR3 of humanized murine anti-human B7-2 heavy chain

<220>
<221> CDS
<222> (1)..(21)

<400> 13
gcg gcc tgg tat atg gac tac 21
Ala Ala Trp Tyr Met Asp Tyr
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<210> 14
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR3 of humanized murine anti-human B7-2 heavy chain

<400> 14
Ala Ala Trp Tyr Met Asp Tyr
1 5

<210> 15
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR1 of humanized murine anti-human B7-2 light chain

B4

<220>
<221> CDS
<222> (1)..(51)

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aaa tcc agt cag agt ctg ctc aac agt aga acc cga gag aac tac ttg 48
Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu
1 5 10 15

gct 51
Ala

<210> 16
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR1 of humanized murine anti-human B7-2 light chain

<400> 16
Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu
1 5 10 15

Ala

<210> 17
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR2 of humanized murine anti-human B7-2 light chain

<220>
<221> CDS
<222> (1)..(21)

<400> 17
tgg gca tcc act agg gaa tct 21
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 18
<211> 7
<212> PRT
<213> Artificial Sequence

B4

<220>
<223> Description of Artificial Sequence: CDR2 of humanized murine anti-human B7-2 light chain

<400> 18
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 19
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR3 of humanized murine anti-human B7-2 light chain

<220>
<221> CDS
<222> (1)..(24)

<400> 19
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Thr Gln Ser Tyr Asn Leu Tyr Thr
1 5

<210> 20
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CDR3 of humanized murine anti-human B7-2 light chain

<400> 20
Thr Gln Ser Tyr Asn Leu Tyr Thr
1 5

<210> 21
<211> 1960
<212> DNA
<213> Mus sp.

<220>
<221> CDS
<222> (12)..(408)

<220>
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<400> 21
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1 5 10

B4

tgg gta tct ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat 98
Trp Val Ser Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp
15 20 25

tcc ctg gct gta agc tta gga gag agg gcc act att agc tgc aaa tcc 146
Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser
30 35 40 45

agt cag agt ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg 194
Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp
50 55 60

tac cag cag aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca 242
Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
65 70 75

tcc act agg gaa tct ggg gtc cct gat cgc ttc agt ggc agt gga tct 290
Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
80 85 90

ggg aca gat ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg 338
Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val
95 100 105

gca gtt tat tac tgc agc caa tct tat aat ctt tac acg ttc gga cag 386
Ala Val Tyr Tyr Cys Ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln
110 115 120 125

ggg acc aag gtg gaa ata aaa c gtaagtagtc ttctcaactc tagaaattct 438
Gly Thr Lys Val Glu Ile Lys
130

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agaactttat taaggaatag ggggaagcta ggaagaaact caaaacatca agattttaaa 618

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aacaccatcc tgtttgcttc tttcctcag ga act gtg gct gca cca tct gtc    790
                              Arg Thr Val Ala Ala Pro Ser Val
                                  135                 140

ttc atc ttc ccg cca tct gat gag cag ttg aaa tct gga act gcc tct   838
Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
                145                 150                 155

gtt gtg tgc ctg ctg aat aac ttc tat ccc aga gag gcc aaa gta cag   886
Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
            160                 165                 170

tgg aag gtg gat aac gcc ctc caa tcg ggt aac tcc cag gag agt gtc   934
Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
        175                 180                 185

aca gag cag gac agc aag gac agc acc tac agc ctc agc agc acc ctg   982
Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
    190                 195                 200

acg ctg agc aaa gca gac tac gag aaa cac aaa gtc tac gcc tgc gaa   1030
Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
205                 210                 215                 220

gtc acc cat cag ggc ctg agc tcg ccc gtc aca aag agc ttc aac agg   1078
Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
                225                 230                 235

gga gag tgt tagagggaga agtgccccca cctgctcctc agttccagcc           1127
Gly Glu Cys

tgaccccctc ccatcctttg gcctctgacc ctttttccac aggggaccta cccctattgc 1187

ggtcctccag ctcatctttc acctcacccc cctcctcctc cttggcttta attatgctaa 1247

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B4

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catgatataa aataacaaca caataaaagc aattaaataa acaaacaata gggaaatgtt 1727

taagttcatc atggtactta gacttaatgg aatgtcatgc cttatttaca tttttaaaca 1787

ggtactgagg gactcctgtc tgccaagggc cgtattgagt actttccaca acctaatttta 1847

atccacacta tactgtgaga ttaaaaacat tcattaaaat gttgcaaagg ttctataaag 1907

ctgagagaca aatatattct ataactcagc aatcccactt ctaggatcaa ttc 1960

<210> 22
<211> 239
<212> PRT
<213> Mus sp.

<400> 22

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser
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20 25 30

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
35 40 45

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
50 55 60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
100 105 110

Tyr Cys Ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
115 120 125

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
130 135 140

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
145 150 155 160

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
165 170 175

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
180 185 190

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
195 200 205

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
210 215 220

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 23
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<212> DNA
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<220>
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<222> (12)..(417)

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B4

<220>
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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr
1 5 10

gct aca ggt gtg cac tcc cag gtc cag ctg gtg cag tct ggg gct gag 98
Ala Thr Gly Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu
15 20 25

gtg aag aag cct ggg agc tca gtg aag gtg tcc tgc aaa gct tcc ggc 146
Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly
30 35 40 45

tac aca ttc act gat tat gct ata cag tgg gtg aga cag gct cct gga 194
Tyr Thr Phe Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly
50 55 60

cag ggc ctc gag tgg att gga gtt att aat att tac tat gat aat aca 242
Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr
65 70 75

aac tac aac cag aag ttt aag ggc aag gcc aca atg act gta gac aag 290
Asn Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys
80 85 90

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tcg acg agc aca gcc tat atg gaa ctt agt tct ttg aga tct gag gat   338
Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp
 95                 100                 105

acg gcc gtt tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg   386
Thr Ala Val Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp
110                 115                 120                 125

ggt caa ggt acc ctt gtc acc gtc tcc tca g gtgagtcctt aaaacctcta   437
Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                130                 135

gagctttctg gggcgagccg ggcctgactt tggctttggg gcagggagtg ggctaaggtg 497

aggcaggtgg cgccagccag gtgcacaccc aatgcccgtg agcccagaca ctggaccctg 557

cctggaccct cgtggataga caagaaccga ggggcctctg cgccctgggc ccagctctgt 617

cccacaccgc ggtcacatgg caccacctct cttgcag cc tcc acc aag ggc cca   671
                                    Ala Ser Thr Lys Gly Pro
                                                    140

tcg gtc ttc ccc ctg gcg ccc tgc tcc agg agc acc tcc gag agc aca   719
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
            145                 150                 155

gcg gcc ctg ggc tgc ctg gtc aag gac tac ttc ccc gaa ccg gtg acg   767
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
        160                 165                 170

gtg tcg tgg aac tca ggc gct ctg acc agc ggc gtg cac acc ttc cca   815
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
    175                 180                 185

gct gtc cta cag tcc tca gga ctc tac tcc ctc agc agc gtg gtg acc   863
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
190                 195                 200                 205

gtg ccc tcc agc aac ttc ggc acc cag acc tac acc tgc aac gta gat   911
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
                210                 215                 220

cac aag ccc agc aac acc aag gtg gac aag aca gtt g gtgagaggcc      958
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
            225                 230

agctcaggga gggagggtgt ctgctggaag ccaggctcag ccctcctgcc tggacgcacc 1018

ccggctgtgc agccccagcc cagggcagca aggcaggccc catctgtctc ctcacccgga 1078

ggcctctgcc cgccccactc atgctcaggg agagggtctt ctggcttttt ccaccaggct 1138

ccaggcaggc acaggctggg tgcccctacc ccaggccctt cacacacagg ggcaggtgct 1198

tggctcagac ctgccaaaag ccatatccgg gaggaccctg cccctgacct aagccgaccc 1258

caaaggccaa actgtccact ccctcagctc ggacaccttc tctcctccca gatccgagta 1318
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B4

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actcccaatc ttctctctgc ag ag cgc aaa tgt tgt gtc gag tgc cca ccg   1369
                         Glu Arg Lys Cys Cys Val Glu Cys Pro Pro
                             235                 240

tgc cca g gtaagccagc ccaggcctcg ccctccagct caaggcggga caggtgccct  1426
Cys Pro
    245

agagtagcct gcatccaggg acaggccccc gctgggtgct gacacgtcca cctccatctc 1486

ttcctcag ca cca cct gcg gca gca ccg tca gtc ttc ctc ttc ccc cca   1535
        Ala Pro Pro Ala Ala Ala Pro Ser Val Phe Leu Phe Pro Pro
                    250                 255

aaa ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc acg tgc   1583
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
260                 265                 270                 275

gtg gtg gtg gac gtg agc cac gaa gac ccc gag gtc cag ttc aac tgg   1631
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp
                280                 285                 290

tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag cca cgg gag   1679
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
            295                 300                 305

gag cag ttc aac agc acg ttc cgt gtg gtc agc gtc ctc acc gtt gtg   1727
Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val
        310                 315                 320

cac cag gac tgg ctg aac ggc aag gag tac aag tgc aag gtc tcc aac   1775
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
    325                 330                 335

aaa ggc ctc cca gcc ccc atc gag aaa acc atc tcc aaa acc aaa g     1821
Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys
340                 345                 350

gtgggacccg cggggtatga gggccacatg gacagaggcc ggctcggccc accctctgcc 1881

ctgggagtga ccgctgtgcc aacctctgtc cctacag gg cag ccc cga gaa cca   1935
                                        Gly Gln Pro Arg Glu Pro
                                        355                 360

cag gtg tac acc ctg ccc cca tcc cgg gag gag atg acc aag aac cag   1983
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
                365                 370                 375

gtc agc ctg acc tgc ctg gtc aaa ggc ttc tac ccc agc gac atc gcc   2031
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
            380                 385                 390

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc aca   2079
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
        395                 400                 405
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cct ccc atg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc   2127
Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
    410                 415                 420

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc   2175
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
425                 430                 435                 440

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc   2223
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
                445                 450                 455

ctg tcc ccg ggt aaa tgagtgaatt c                                 2249
Leu Ser Pro Gly Lys
            460
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<210> 24
<211> 461
<212> PRT
<213> Mus sp.

<400> 24

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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
  1               5                  10                  15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45

Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
    50                  55                  60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
65                  70                  75                  80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
                85                  90                  95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
    130                 135                 140

Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190
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B4

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Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu
225                 230                 235                 240

Cys Pro Pro Cys Pro Ala Pro Pro Ala Ala Ala Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460
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B4